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Rasmussen syndrome: an atypical presentation in ten patients

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ABSTRACT – *Aim.* The aim of this study was to analyse the electroclinical and imaging findings and outcome of patients with Rasmussen syndrome (RS) with atypical manifestations.
Methods. We conducted a retrospective, descriptive study of 10 of 44 consecutive patients with RS with atypical features, followed between 1999 and 2017.
Results. Six patients were boys and four were girls. The mean and median ages at onset of the seizures were 8.8 and 6.5 years, respectively (range: 4.6-13 years). All of the patients except one had seizures. Eight patients (80%) had *epilepsia partialis continua* that started at a mean age of 7.5 years (range: 7-15 years). In our series, hemiparesis without seizures was the first manifestation in three patients, one of whom had dual pathology. In two patients, the first manifestation was dyskinetic movements, followed by delayed-onset seizures associated with unilateral caudate atrophy. Two patients had a focal lesion mimicking focal cortical dysplasia as the first MRI abnormality; one of these two patients had epileptic spasms in clusters. Bilateral cerebral hemisphere involvement was observed in three patients during the course of the disease. Six of eight patients responded well to surgical treatment.
Conclusion. Progressive hemiparesis alone or with delayed-onset seizures, dyskinetic movements associated with seizures, a focal lesion mimicking focal cortical dysplasia, and bilateral brain involvement were the atypical features recognized. Our series of patients responded well to surgery. Clinical, video-EEG, and neuroradiological follow-up is important for early confirmation of RS in order to initiate adequate management of the condition.

Key words: atypical, epilepsia partialis continua, encephalitis, immune, hemiparesis, dyskinesia, caudate atrophy

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Rasmussen *et al*. (1958) reported three patients suffering from focal seizures secondary to chronic localized encephalitis. Most researchers and epileptologists still use the term "Rasmussen encephalitis" or "Rasmussen syndrome" for this particular condition (Granata, 2003; Bien *et al*., 2005; Granata *et al*., 2012). Here, we prefer to use the name Rasmussen syndrome (RS) for the entity in recognition of Rasmussen's contribution.

RS is a rare and severe immune-mediated brain disorder resulting in unilateral brain atrophy and leading to progressive neurological dysfunction and refractory seizures (Rasmussen *et al*., 1958; Bien *et al*., 2005). Different mechanisms have been suggested, however, the aetiopathogenesis is not fully understood (Rogers *et al*., 1994; Schwab *et al*., 2009).

The entity has been described as "distinctive constellations" based on specific lesions that are not clearly defined as electroclinical syndromes (Berg *et al*., 2010). This is a diagnostically meaningful category of epilepsy which may have therapeutic implications, particularly for surgery.

Most patients with RS are refractory to conventional antiepileptic drugs (AEDs) and the only recommended therapeutic approach is surgical hemispherectomy, which either removes substantial parts of the affected hemisphere or disconnects the hemispheres while removing a minimal amount of cortical structures (Villemure *et al*., 1991; Tubbs *et al*., 2005; Marras *et al*., 2010; Caraballo *et al*., 2011; Olson *et al*., 2013).

In the literature, patients with atypical features have been reported (Hart *et al*., 1998; Firlik *et al*., 1999; Frucht, 2002; Tobias *et al*., 2003; Bien *et al*., 2007; Ferrari *et al*., 2011; O'Rourke *et al*., 2014; Yang and Sun, 2016). Some cases manifest with absence or delayed-onset seizures, unusual events, such as epileptic spasms and hemidystonic episodes, headache as the initial manifestation, dual pathology, and bilateral brain involvement. Dual pathology may be seen in 10% of patients and varies from low-grade tumour, cortical dysplasia, tuberous sclerosis, mesial temporal sclerosis, vascular abnormalities, to early ischaemic lesions (Yacubian *et al*., 1996; Hart *et al*., 1998; Granata *et al*., 2012).

New knowledge has contributed to our understanding of the pathophysiology, diagnosis, and management of the condition (Olson *et al*., 2013). A consensus for the diagnosis and therapy of RS, defined at the sixth European Congress on Epileptology in Vienna in 2004, has been published (Bien *et al*., 2005). Bien *et al*. (2013) reported an incidence rate of 3.3 new cases with RS in Germany per year.

The aim of this study was to analyse the electroclinical and neuroradiological features and outcome of patients with RS with an atypical presentation.

Material and methods

We conducted a retrospective, descriptive study of 10 of 44 patients with RS, followed between March 1990 and June 2017 at the Garrahan Hospital of Buenos Aires, Argentina.

For our first three patients, included in the study by Hart *et al*. (1994), and the following 28 previously published cases (Caraballo *et al*., 1998), we used the inclusion criteria according to Hart *et al*. (1994). From 2004, the inclusion criteria, as defined by Bien *et al*. (2005) from the consensus group, were considered.

Inclusion criteria

A. Children who developed epilepsia partialis continua (EPC) and met at least one of the following criteria to suggest the diagnosis of chronic encephalitis:

– progressive neurological deficit at the beginning or after the onset of epilepsia partialis continua, but before the start of treatment;

– progressive hemispheric atrophy on CT, MRI, or both, with or without density or signal abnormalities;

– presence of oligoclonal or monoclonal banding;

– or biopsy evidence of chronic encephalitis.

B. Children who did not have *epilepsia partialis continua* but had focal epilepsy and biopsy evidence of chronic encephalitis. They may, in addition, have met Criteria 1, 2, or 3 (Bien *et al*., 2005).

Bien *et al*. have divided the criteria into two parts. RS is diagnosed when either all three criteria of Part A or two out of three criteria of Part B are met. We first checked the features of Part A, and if these were not present, features of Part B were taken into account.

Part A.

1. Clinical: focal seizures (with or without EPC) and unilateral cortical deficits.
2. EEG: unihemispheric slowing with or without epileptiform activity and unilateral seizure onset.
3. MRI: unihemispheric focal cortical atrophy and at least one of the following: a hyperintense signal in the grey or white matter on T2/Flair or a hyperintense signal, or atrophy of the ipsilateral caudate head.

Part B.

1. Clinical: EPC or progressive unilateral cortical deficits.
2. MRI: progressive unihemispheric focal cortical atrophy.

Progressive means that at least two sequential clinical examinations or MRI studies are required to meet the respective criteria. To indicate clinical progression, each of these examinations must document a neurological deficit, and this must increase over time. To

indicate progressive hemiatrophy, each of these MRIs must show hemiatrophy, and this must increase over time.
3. Histopathology: T-cell-dominated encephalitis with activated microglial cells (typically, but not necessarily, forming nodules). Numerous parenchymal macrophages, B cells, or plasma cells or viral inclusion bodies exclude the diagnosis of RS.
In addition, if no biopsy is performed, MRI with administration of gadolinium and brain CT scan should be performed to document the absence of gadolinium enhancement and calcifications to rule out the differential diagnosis of unihemispheric vasculitis.
Other immune-mediated epileptic encephalopathies, *i.e.* cerebral vasculitis including lupus erythematosus, subacute measles encephalitis with or without immunodeficiency, hemiconvulsion-hemiplegia-epilepsy syndrome, focal cortical dysplasia including hemimegalencephaly, tumour, stroke, Sturge-Weber syndrome, and neurometabolic diseases, particularly mitochondriopathies, were excluded. Most of these entities may be associated with EPC.
In this study all patients underwent video-EEG in addition to the routine EEG recordings. Evoked potentials, repeated brain CT scans, and MRIs with or without gadolinium were obtained in all patients. Magnetic resonance spectroscopy was performed in five. Neurometabolic studies, especially to rule out mitochondrial disease, were also performed in all cases. CSF studies including oligoclonal bands were performed in four patients, and a measles antibody test was performed in five. Other studies, such as liver function, and blood and autoantibody tests, were also performed. N-methyl-D-aspartate (NMDA), alpha amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), leucine-rich-glioma protein (1 LGI1), glutamic acid decarboxylase (GAD) antibody, and antinuclear antibody (ANA) screening, as well as mitochondrial DNA testing for mutations, were performed for all patients. Brain biopsy was performed for four patients before surgery treatment.
Data on school achievements and neuropsychological evaluations (Terman-Merrill or WISC III or IV) were repeatedly obtained during the follow-up of two to 20 years. In the cases in which formal neuropsychological tests could not be performed, cognitive changes were evaluated based on clinical judgment.

Results

General characteristics

Seven patients (70%) had a history of infectious disease previous to epilepsy onset. In five patients, the infectious episode had occurred one and a half months previously and in two others two months before the onset of the seizures.
Brain biopsy, performed in four patients, was compatible with RS in all except one, and bilateral involvement was observed in three of them. Pathology findings of RS may be fairly variable from patient to patient, related to the activity of the disease. Pathology samples were available for eight of our patients, showing typical neuronal loss, abundant lymphocytic infiltration in the perivascular spaces, and numerous microglial nodules both within the cortex and in the deeper white matter in three. In our series, there were no patients with a non-inflammatory condition. In one patient, dual pathology was identified, which was suggestive of ischaemic brain injury.
In *table 1*, the clinical, EEG, and neuroradiological features, CFS antibody and neurometabolic study results, and surgical treatment are listed.

Clinical features

The mean and median ages at onset of the seizures were 8.8 and 6.5 years, respectively (range: 4.6-13 years). All of the patients except one had focal motor seizures, with secondary generalization in five patients (50%); two patients (20%) had somatosensory focal seizures, four patients (40%) had generalized tonic seizures, and one (10%) had complex focal seizures. Simple focal seizures were always contralateral to the affected hemisphere. Six patients (60%) had focal motor and three patients (30%) had generalized status epilepticus. Eight patients (80%) had EPC that had started at a mean age of 7.5 years (range: 7-15 years). In two patients (20%), focal motor seizures were the first manifestation, preceded by hemidystonic and hemidyskinetic movements. One patient had epileptic spasms in clusters (*figure 1*). EPC lasted between 26 hours and six months.

Neurological symptoms other than epilepsy

In the first stages of the disease, hemiparesis was sometimes secondary to Todd's paresis, but became persistent, fluctuating in severity according to the increase of the seizures in all cases, except three. The definitive neurological deficit (hemiparesis) occurred within the first year after onset of the seizures in three patients (30%), in the second or third year after seizure onset in four patients (40%), and more than three years after seizure onset in three patients (19%). Hemiparesis was the first manifestation in three patients. Severe hemiparesis lead four patients to become wheelchair bound. Dysphasia and dysarthria were found in four patients (40%), and visual deficits were observed in two (20%).

Table 1. The clinical, EEG, and neuroradiological features, CFS antibody and neurometabolic study results, and surgical treatment of our 10 patients with Rasmussen syndrome.

Patient	Age (years) at onset / sex	Clinical features at onset	Age at onset of EPC (years)	Cerebrospinal fluid		EEG	MRI Findings	Surgical treatment: functional hemispherectomy
				Oligoclonal bands	Anti-GAD, AMPA, LGI1, ANA			
1	5 / M	Left hemiparesis Focal seizures	7.5	-	-	Focal discharges Unilateral disturbance of background rhythm	Atrophy with T2/FLAIR hypersignal in medial aspect of thalamus, caudate, and occipital lobe in the right hemisphere Suggestive of ischaemic brain injury	Yes
2	9 / M	Right hemiparesis predominantly in upper limbs	10.5	-	-	Frequent spikes and slow waves, almost continuous in the left hemisphere	No brain atrophy Dorsolateral left frontal T2/FLAIR hypersignal in subcortical white matter with mild swelling and CSF space effacement	Yes
3	13 / F	Left focal seizures and left hemiparesis. After surgery, bilateral independent focal seizures	15	-	-	Right focal discharges: frontal spikes and spikes and slow waves	Confluent and subcortical FLAIR/T2 hyperintense lesions in the right superior frontal gyrus (pre-motor region) with partial effacement of surrounding CSF spaces Contralateral hemisphere involvement after 10 months	Yes
4	7 / F	Focal seizures and hemiparesis. After surgery, bilateral independent focal seizures	9	-	-	Diffuse slow waves Multifocal independent spikes	Enlargement of the bilateral ventricles and cerebrospinal fluid space over the convexities of the frontoparietal lobes, compared with previous studies	No

Table 1. The clinical, EEG, and neuroradiological features, CFS antibody and neurometabolic study results, and surgical treatment of our 10 patients with Rasmussen syndrome (*Continued*).

Patient	Age (years) at onset / sex	Clinical features at onset	Age at onset of EPC (years)	Cerebrospinal fluid		EEG	MRI Findings	Surgical treatment: functional hemispherectomy
				Oligoclonal bands	Anti-GAD, AMPA, LGI1, ANA			
5	6 / M	Left hemiparesis Focal seizures and epileptic spasms	7	-	-	Diffuse background slowing, more marked in the right hemisphere, and frequent sharp waves over the right frontotemporal region Bursts of high-voltage, generalized, symmetric slow waves, superimposed on spikes, ranging from 0.5-2 seconds in duration	Localized T2/FLAIR subcortical hypersignal in the right frontoparietal areas, suggestive of focal cortical dysplasia	Yes
6	8 / F	Hemichorea/ hemidystonia Hemiparesis progresiva and focal seizures	10	-	-	Asymmetric background activity, right central sharp waves	T2/FLAIR hypersignal in the right caudate and right cerebral hemiatrophy	No
7	5 / M	Focal seizures and hemiparesis	8.5	-	-	Frequent slow waves and spike discharges in the right hemisphere	Localized T2/FLAIR subcortical hypersignal in right frontoparietal areas	Yes
8	12 / M	Episodes of focal seizures and hemiparesis	-	-	-	Slow waves, spikes, and polyspikes in the right hemisphere	Localized T2/FLAIR subcortical hypersignal in right areas, suggestive of focal cortical dysplasia and progressive right hemicerebral atrophy	Yes
9	8 / F	Focal seizures from both hemispheres independently and progressive hemiparesis	10	-	-	Focal and generalized paroxysms	Progressive right hemicerebral atrophy and hypersignal focal lesion in the left parietal lobe and right frontal lobe	No
10	6 / M	Focal seizures and hemidystonia	-	Not done	Not done	Focal paroxysms	T2/FLAIR hypersignal in left striatum, followed by left cerebral hemiatrophy	No

EPC: epilepsia partialis continua.

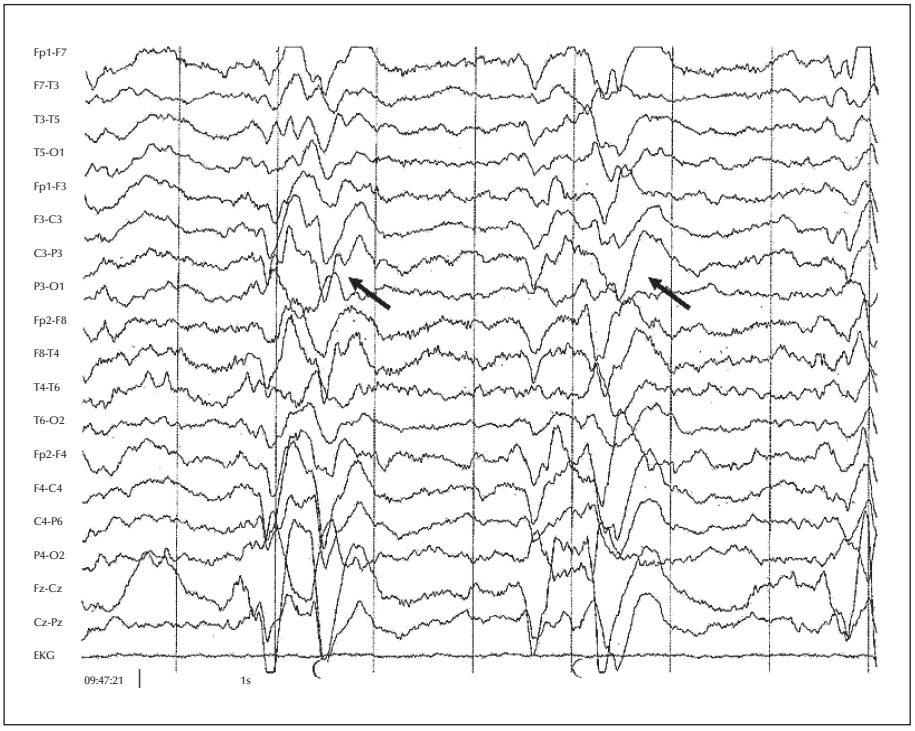

Figure 1. The ictal EEG recording shows diffuse high-voltage slow-wave paroxysms associated with periodic spasms (see arrow).

Cognitive impairment and behavioural disturbances were additional neurological manifestations that were observed in all patients. Irritability, hyperactivity, and emotional lability were the most frequent behavioural changes. In the first three years after seizure onset, the patients were found to have learning difficulties, memory loss, and attention deficits.

EEG findings

The background activity in the affected hemisphere showed delta and theta slow waves and sleep disorganization in all patients. Over time, the slow activities became bilateral, but appeared predominantly in the affected hemisphere in eight patients. In the early period, the interictal EEG showed focal epileptiform abnormalities in one hemisphere in six patients (60%) and multifocal abnormalities in four patients (40%). The multifocal abnormalities were seen in one hemisphere in two patients. Over time, the interictal EEG recordings showed further deterioration; the epileptiform activity increased and started to involve the contralateral hemisphere as well. Synchronous bilateral spikes were observed in one patient (10%).
The ictal EEG showed a multifocal origin, but was confined to the affected hemisphere in all patients. In three of the 10 patients, seizure onset was registered in the unaffected hemisphere as well.

Neuroradiological findings

CT and MRI demonstrated progressive unilateral cerebral atrophy in five patients and bilateral atrophy in one. In the early stages of the disease, an abnormal cortical and/or subcortical hyperintense signal on T2 and Flair images was observed in six patients; in two of them, the focal lesion mimicked focal cortical dysplasia (*figure 2*). T2 hyperintensity and atrophy in the basal ganglia, particularly in the caudate nucleus, were documented in three patients (*figure 3*), one of whom had atrophy in the occipital lobe in the right hemisphere, suggestive of ischaemic brain injury.
Three patients had bilateral brain involvement (*figure 4*). Magnetic resonance spectroscopy showed decreased N-acetyl-D-aspartate signal intensity over the entire affected hemisphere in two patients. Functional imaging was not performed for any of the patients in this series.

Laboratory tests

Neurometabolic studies for blood and urine were normal in all cases. Cerebrospinal fluid was normal in nine patients (90%). Oligoclonal bands were positive in one patient. Antibodies were normal in all patients and mitochondrial DNA genetic testing for mutations did not show abnormalities in three patients.

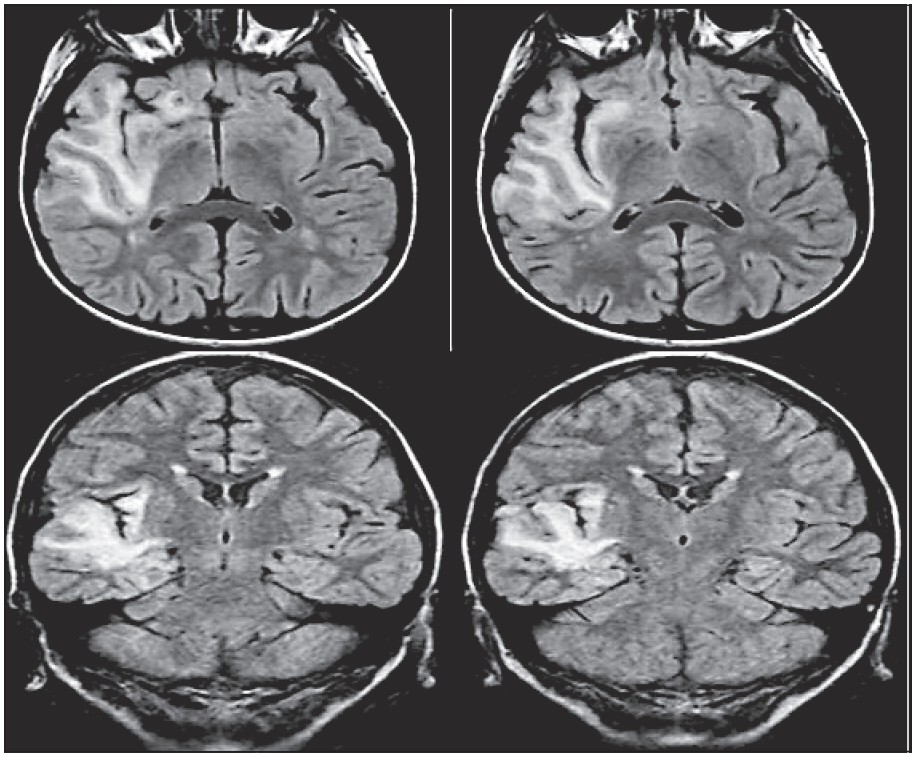

Figure 2. Subcortical FLAIR/T2 hyperintense lesions in the right upper frontal pre-motor region mimicking focal cortical dysplasia.

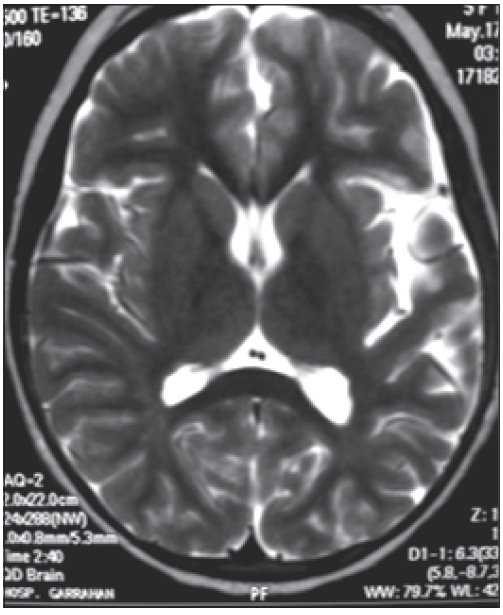

Figure 3. Hyperintensity of basal ganglia and asymmetric Sylvian fissures with left enlarged subarachnoid spaces.

Treatment

The seizures were refractory to all different schemes of classic and new AEDs used. None of the AEDs prevented progression of the disease. High-dose prednisone (2-3 mg/kg/day) was indicated for a period of between seven and 30 months in nine patients, and intravenous immunoglobulin, for three days at 400 mg/kg/day, administered monthly, was administered in all 10 patients for eight to 25 months. Corticosteriods combined with immunoglobulins were used in five patients for a period of seven to 25 months. Five of 10 patients receiving this combination improved in terms of seizure frequency as well as progressive deterioration. EPC disappeared in three of nine patients.

Two patients received the ketogenic diet (KD) for six and 24 months, respectively. In both patients, a 50-74% seizure reduction was achieved. In the patients with bilateral brain involvement, a vagus nerve stimulation device was implanted and a 50% seizure reduction was achieved after 24 months of follow-up.

Other immunomodulatory treatments, such as monoclonal antibodies, plasmapheresis, and immunosuppressive drugs as well as antiviral treatments, were not indicated in our series of patients. The patient (Patient 4 in *table 1*) with bilateral brain involvement and the patient (Patient 10) without hemiparesis with a good response to the KD did not meet the criteria for surgery. Surgical treatment was performed after hemiparesis had become fixed in eight patients.

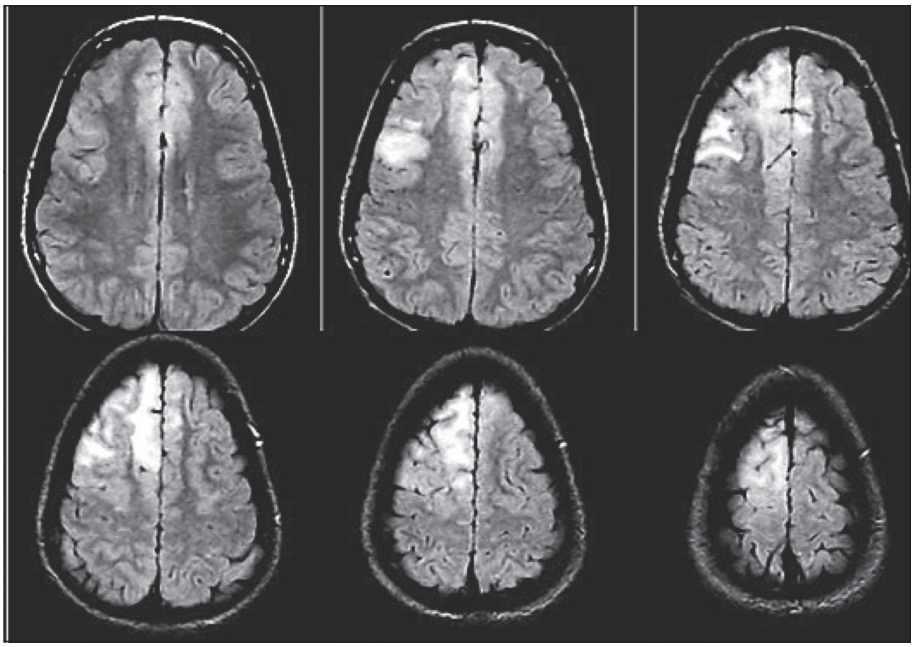

Figure 4. Bilateral Rasmussen syndrome: confluent and subcortical FLAIR/T2 hyperintense lesions in the right upper frontal pre-motor region with partial collapse of surrounding arachnoid spaces. After 10 months, there was contralateral involvement.

Outcome

At the last control, after a mean of seven years of follow-up (range: 2 to 15 years), good surgical outcome (Engel Class Ia) was observed in six of eight patients who had undergone surgery. In two of eight patients who underwent surgery, seizures continued; both had bilateral and independent electroclinical features as well as neuroradiological imaging of bilateral brain involvement and pathological findings compatible with RS. In these two patients (Patients 3 and 9), bilateral brain involvement was seen on neuroradiological imaging after surgery. Hemiparesis remained unchanged in all patients who received surgery, except for fine finger movements, which deteriorated in four and improved in one of eight patients. All patients developed independent gait after surgery. The outcome for visual fields remained unchanged if already impaired or worsened following surgery.

Dysphasia improved during follow-up in four patients. All children who became seizure-free improved motor, neuropsychological, and behavioural performance. Quality of life improved in all patients who became seizure-free and AEDs could be reduced in all six patients who responded well to surgery.

One patient who did not undergo surgery (Patient 9) and two patients (Patients 3 and 4) who were refractory to surgical treatment and who subsequently were shown to have bilateral brain involvement continued having refractory seizures after two, six, and 10 years of follow-up, respectively. The remaining patient (Patient 10) who did not undergo surgery and did not have hemiparesis is still on the KD with a 50-75% seizure reduction.

Discussion

Here we present a series of 10 patients who met the diagnostic criteria for RS with atypical electroclinical and neuroradiological manifestations, with a good response to surgical treatment in six of eight patients. These six patients had unilateral brain involvement, while the remaining two turned out to have bilateral involvement. The presence of refractory unilateral focal and multifocal seizures, EPC, and progressive neurological and neuroradiological involvement of one hemisphere is suggestive of RS.

Early recognition is crucial to initiate adequate therapeutic management of this severe epileptic syndrome. RS is the most frequent progressive syndrome associated with EPC.

RS is a rare syndrome with peak incidence at the age of six years, characterized by refractory seizures, often associated with EPC and clinical manifestations of progressive hemispheric dysfunction. Imaging studies show progressive, usually unilateral, cerebral atrophy. In our series of patients, the first manifestations of the disease were hemiparesis without seizures in three

patients, dyskinetic movements without seizures associated with unilateral caudate atrophy in two, and a focal lesion mimicking focal cortical dysplasia on MRI in two. The three remaining patients had bilateral hemispheric involvement during the course of the disease.

Formal diagnostic criteria for RS were first proposed by Hart *et al*. (1995), and our group participated in this interesting collaborative study. Subsequently, the European consortium compounded these criteria with new data from advanced neuroimaging techniques that better characterized the morphological aspects of the disease (Bien *et al*., 2005). The clinical criteria proposed include a two-step diagnostic approach. If the hallmark clinical, EEG, and imaging criteria are fully met, the diagnosis may be established without the need for a brain biopsy, however, if the criteria are not fulfilled, the progression of clinical deficits must be associated with progressive hemispheric atrophy, as documented by sequential MRI or alternatively by characteristic histopathological findings (Chiapparini *et al*., 2003; Granata *et al*., 2003a, 2012). It was stressed that the progression of the neurological deficit and the worsening of unilateral brain damage must be confirmed in at least two sequential examinations, and when a brain biopsy is not performed, MRI with gadolinium and CT are required to rule out unihemispheric vasculitis. The later inclusion criteria for the diagnosis of RS proposed (Bien *et al*., 2005) are more inclusive compared with the previous ones. Nevertheless, further discussion of the inclusion criteria may be necessary in order to make them as effective as possible for early diagnosis of the syndrome and facilitate the planning of adequate medical and surgical treatment. Finally, an accurate diagnostic work-up should rule out all the conditions characterized by unilateral neurological syndromes or EPC, as well as inflammatory diseases mimicking RS (Granata *et al*., 2012).

In the literature, patients with delayed seizure onset have been published (Bien *et al*., 2007). In these cases, hemiparesis was the initial manifestation with or without delayed-onset seizures. In the three cases of this series who started with hemiparesis, two had delayed-onset seizures and the remaining patient did not have seizures.

On MRI, the different stages of the disease are cortical swelling with a hyperintense T2/FLAIR signal (Stage 1), followed by a normal volume and a hyperintense signal (Stage 2), atrophy and a hyperintense signal (Stage 3), and finally progressive atrophy with a normal signal (Stage 4) (Granata *et al*., 2003b, 2012). Atrophy and signal change are most prominent in the perisylvian region. Other findings include atrophy of the ipsilateral head of the caudate nucleus in the majority of cases.

Truly bilateral RS is rare. In our two cases, based on the persistent MRI finding of blurring of the grey-white matter junction in the precentral gyrus, in the absence of other neuroimaging changes typical of RS, cortical dysplasia was diagnosed. In a case reported in the literature, an area of hypometabolism in the left precentral gyrus seen on FDG-PET further suggested a focal lesion (O'Rourke *et al*., 2014). In another case, epileptic spasms associated with RS were described; the epileptic spasms were the first manifestation of the syndrome (Ferrari *et al*., 2011). In one of the patients presented here, periodic spasms were recognized during the course of the disease.

In our series of patients, three had bilateral brain involvement. In two of them, the contralateral hemisphere became affected after the hemispherectomy, and in the other, bilateral cerebral involvement occurred in the first stages of the disease. In cases with bilateral cerebral involvement, dual pathology should be ruled out.

The most effective medical treatment to improve seizure control and neurological deterioration are oral and intravenous corticosteroids, however, long-term efficacy has not been confirmed (Bien and Schramm, 2009, 2013; Caraballo *et al*., 2013, Varadkar *et al*., 2014). Intravenous immunoglobulins have also been reported to be effective in a large number of patients with RS (Bien *et al*., 2013; Varadkar *et al*., 2014). The use of a combination of corticosteroids and immunoglobulins has also been used as a treatment option with good response (Granata *et al*., 2012; Bien *et al*., 2013).

Hemispherectomy and hemispherotomy have been shown to be effective in controlling seizures and motor and mental deterioration in over 80% of patients (Villemure *et al*., 1991; Marras *et al*., 2010; Caraballo *et al*., 2011, 2013). After surgery, partial recovery from neurological deficits is seen in the majority of the patients with a significant improvement in their quality of life (Pulsifer *et al*., 2004; Tubbs *et al*., 2005). In our series, results of surgery were good in 75% of the patients. This percentage was lower than that reported in the literature as two of these atypical cases had bilateral brain involvement.

Adolescent and adult patients are increasingly being recognized and account for around 10% of the cases (Hart *et al*., 1997; Granata *et al*., 2012). This form is milder with a more protracted clinical course. Seizures as well as motor and mental deterioration are less severe than in typical childhood RS (Villani *et al*., 2006). Persistently focal RS in adolescents and adults without severe motor deficits or episodes of EPC or status epilepticus have also been reported (Gambardella *et al*., 2008), however, rare cases may have a severe course, similar to that of the childhood form (Granata *et al*., 2012).

We observed basal ganglia involvement in three patients. RS with hemiparesis and prominent basal ganglia involvement and predominant movement disorders associated with contralateral brain MRI abnormalities has been described, and may lead to misdiagnosis (Frucht, 2002; Bien *et al*., 2005; Granata *et al*., 2012; Caraballo *et al*., 2013).
The evolution towards bilateral involvement of the brain in patients does not necessarily occur in the first months of the disease (Tobias *et al*., 2003; Granata *et al*., 2012; Caraballo *et al*., 2013). The bilateral involvement in three patients of our series occurred later; during the course of the syndrome in two.

Conclusion

We present a series of 10 patients who fulfilled the diagnostic criteria for RS with atypical manifestations. Onset of the syndrome was marked by particular clinical features characterized by progressive hemiparesis in three, dyskinetic movements without seizures in two, a focal lesion mimicking focal cortical dysplasia in two, and the remaining three developed bilateral brain involvement during the course of the syndrome. The patients in this series responded well to surgical treatment, as typical cases, except for the two cases with bilateral brain involvement. Clinical, video-EEG, and neuroradiological follow-up is important for early diagnostic confirmation of RS in order to start adequate treatment. □

Disclosures.
None of the authors have any conflict of interest to declare.

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